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BACKGROUND AND AIMS

Alpha-fetoprotein (AFP) is the most widely used biomarker for hepatocellular carcinoma (HCC) patient follow-up, even though around 30% of HCC do not express AFP and its capacity to reliably monitor treatment efficacy is questioned. Interestingly, progastrin, a direct target of the oncogenic Wnt/beta-catenin pathway that is commonly activated in HCC, is secreted as such from tumor cells of various origin, from the very first steps of tumorigenesis. Here, we show the first study evaluating the potency of blood progastrin levels to monitor treatment efficacy and compared it with AFP.



Hepatocellular carcinoma Patients (N=84)

Focal : N=23
Advanced: N=42
Metastatic: N=19

METHODS and PATIENT BLOOD SAMPLES

Systemic treatment (nevarax, tepotinib, regorafenib, nivolumab, anti-FGR or carbozantinib)
and/or
Localized treatment



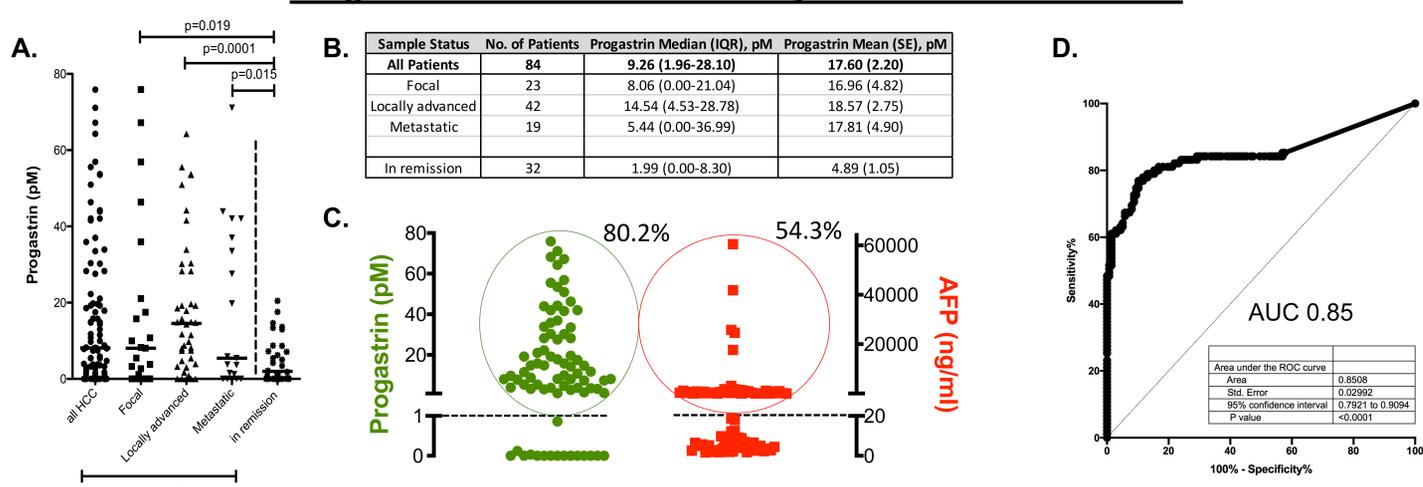
Clinical outcome:

- Progression →
- Decrease →
- Stable →
- Remission R

Progastrin was quantified in the plasma from 84 patients using *CancerREAD* technology (CE marked since 2017). AFP was quantified in the plasma of 79 patients using Cobas E411 (Roche). Variations in the levels of progastrin and AFP were analysed in relationship with evolution of the disease (progression, decrease, stable, in remission) in 48 patients without taking into account the different treatment regimens.

RESULTS

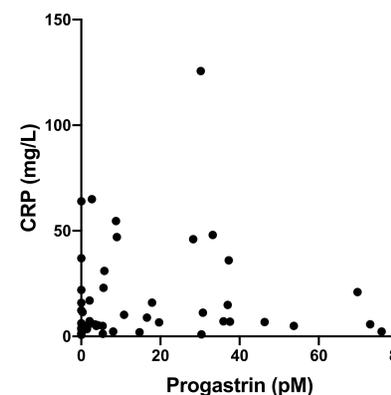
Progastrin has a better sensitivity to detect HCC than AFP



- A. Patients in remission had a significantly lower blood progastrin compared to focal, locally advanced or metastatic HCC. (p=0.019, p=0.0001, p=0.015)
- B. Median and mean values of plasma progastrin in all HCC patients.
- C. AFP was above 20ng/ml in 54.3% of the samples while progastrin was detected in 80.2% (threshold = 1pM).
- D. ROC curve of progastrin for the diagnosis of HCC compared to 137 healthy blood donors (age 18-25 years old). (AUC 0.85)

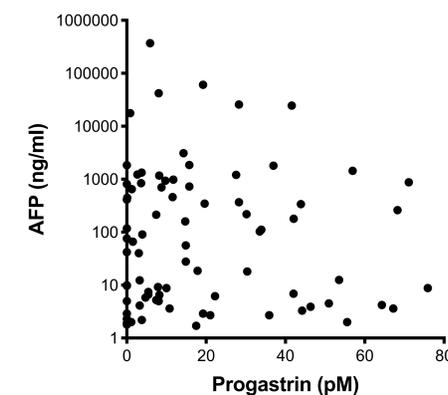
Absence of correlation between Progastrin and CRP levels

Spearman Rhô: 0.26
p = 0.06 (ns)



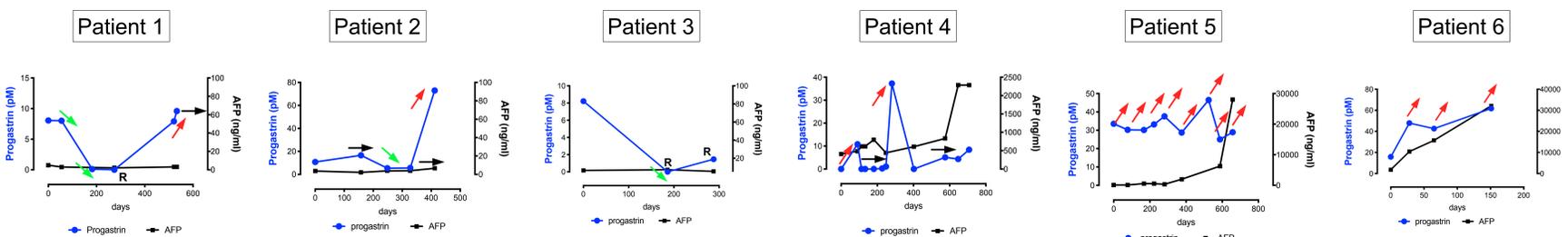
Absence of correlation between Progastrin and AFP levels

Spearman Rhô: 0.034
p = 0.76 (ns)



Progastrin is a biomarker for HCC patient follow-up

- progression
- decrease
- stable
- R Rémission



Longitudinal analyses of both progastrin and AFP levels were assessed in 37 patients. Representative examples of variations in progastrin (in blue) and AFP (in black) levels in blood samples from six patients during follow-up and their significance regarding disease evolution are shown. Progastrin was a better biomarker of the evolution of the disease in 51.4% (representative patients 1-4). Both biomarkers were accurate in 24.3% (representative patients 5-6). AFP was better than progastrin only in 16.2%.

CONCLUSIONS

- Progastrin is a better biomarker than AFP to detect HCC.
- Progastrin is a good biomarker for the follow-up of HCC patients.
- Progastrin could be used in combination with AFP to improve HCC patient follow-up and treatment efficacy monitoring.